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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/571,242

04/30/2007

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1656

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/571,242	<b>Applicant(s)</b> CANTLEY ET AL.	
	<b>Examiner</b> David J. Steadman	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 October 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 12,17,21,22,31,36,40,71 and 72 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12,17,21,22,31,36,40,71 and 72 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of the Application***

- [1]** Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are pending in the application.
- [2]** Applicant's amendment to the claims, filed on 10/13/09, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3]** Applicant's amendment to the specification, filed on 10/13/09, is acknowledged.
- [4]** Receipt of a supplemental application data sheet, filed on 10/13/09, is acknowledged.
- [5]** Applicant's remarks filed on 10/13/09 in response to the non-final Office action mailed on 4/14/09 have been fully considered and are deemed to be persuasive to overcome at least one rejection and/or objection previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [6]** The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

### ***Election/Restriction***

- [7]** Claims 17 and 36 are being examined only to the extent the claims read on the elected species of phenformin. Election was made without traverse in the reply filed on 3/23/09.

### ***Oath/Declaration***

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**[8]** The objection to the declaration under 37 CFR 1.63 as being defective is withdrawn in view of the instant supplemental application data sheet to identify the city and either state or foreign country of residence of each inventor.

### ***Specification/Informalities***

**[9]** The objection to the title of the invention as not being descriptive is withdrawn in view of the instant specification amendment to replace the title with the following title: ---  
Method for Treating Cancer by Increasing AMP-Activated Kinase Activity---.

**[10]** The objection to the description of Figures 5a, 5b, and 5c is withdrawn in view of the instant specification amendment to the description of Figure 5.

### ***Claim Objection***

**[11]** The objection to claims 12, 21, 31, 40, and 71-72 in the recitation of "LKB1" is withdrawn in view of applicant's argument noting that "LKB1" is not an abbreviation. Abbreviations, unless otherwise obvious and/or commonly used in the art, *e.g.*, "DNA", should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

**[12]** The objection to claims 12 and 22 in the recitation of "(cells of)" and "(cells)", respectively, is withdrawn in view of the instant claim amendment.

***Claim Rejections - 35 USC § 112, Second Paragraph***

[13] The rejection of claims 12, 17, 21-22, 31, 36, 40, and 71-72 as being unclear in the recitation of the relative term “reduced...LKB1 activity” is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See [14][a] at p. 5 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: At p. 6 of the instant remarks, applicant argues the claims are not “insolubly ambiguous” and thus satisfy the requirements of 35 U.S.C. 112, second paragraph.

Applicant’s argument is not found persuasive. The scope of those “cancers characterized by reduced...LKB1 activity” in claims 12 and 71 and the scope of those “cells having reduced or absent LKB1 activity” in claims 31 and 72 should be “clear so the public is informed of the boundaries of what constitutes infringement of the patent” (MPEP 2173). However, in the absence of, *e.g.*, a reference level or amount and type of “LKB1 activity”, for comparison to determine whether or not a cancer or cell has reduced LKB1 activity, one of skill in the art is not apprised of the subset of cancers or cells from among all cancers and cells that are intended as being encompassed by the claims. It is clear from applicant’s argument addressing the reference of Shen (instant remarks at pp. 13-14) that it is applicant’s intent that not all cancers have reduced or absent LKB1 activity. However, in comparison to, *e.g.*, a cancer cell line genetically engineered to *highly* overexpress LKB1, any cancers or cells are likely to have reduced or absent LKB1 activity, even those cancers or cells that may have a so-called “normal” level or

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amount of "LKB1 activity". In the interest of compact prosecution, it is suggested that applicant clarify the meaning of the claims by providing a reference level or amount and type of "LKB1 activity".

**[14]** The rejection of claims 12, 17, 21-22, 31, 36, 40, and 71-72 as being incomplete for omitting essential elements as not requiring the cancer or cells to express AMPK is withdrawn in view of applicant's argument, noting that the claim encompasses compounds that increase AMPK activity by inducing its expression.

**[15]** The rejection of claims 21 and 40 as lacking antecedent basis in the recitation of "the mutation" is withdrawn in view of the instant amendment to the claims.

***Claim Rejections - 35 USC § 112, First Paragraph***

**[16]** The written description rejection of claims 12, 17, 21-22, 31, 36, and 40 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See [15] beginning at p. 6 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: Beginning at p. 7 of the instant remarks, applicant argues there was ample knowledge of AMPK activators at the time of the invention, including small organic molecules, peptides, polypeptides, nucleic acids, and fatty acids, as shown by a number of cited references.

Applicant's argument is not found persuasive. The application claims the benefit of domestic priority to provisional applications filed in 2003. However, the references cited in support of applicant's position appear to have been made publicly available only after the time of filing, *i.e.*, 2006 or later. As such, these references do not appear to support applicant's assertion that "there was ample knowledge of AMPK activators...at the time the application was filed". In fact, these references would appear to dispute applicant's position, showing that only *after* the time of filing were such compounds known in the art.

Applicant further argues the disclosed representative species are sufficient to describe all members of the genus of compounds as recited in the claims. According to applicant, the examiner has applied an improper standard in requiring the representative species to include all members of a genus.

Applicant's argument is not found persuasive. Contrary to applicant's position, the examiner has applied a proper standard in analyzing the claimed invention for written description in accordance with 35 U.S.C. 112, first paragraph. As noted in the prior Office action, the genus of "compounds" that increase AMPK activity (claim 12) or activate AMPK (claim 31) encompass small molecule organic compounds, peptides, polypeptides, antibodies, and nucleic acids, which act directly or indirectly to increase AMPK activity or activate AMPK. This interpretation is supported by applicant's instant remarks, noting that activators of AMPK "include small organic molecules, peptides, polypeptides, nucleic acids, and fatty acids" (instant remarks at p. 8, bottom) and includes compounds that, *e.g.*, induce AMPK expression (instant remarks at p. 7,

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middle). For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the *entire* genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. While the specification discloses certain species of compounds that are encompassed by the genus (*e.g.*, p. 11, lines 1-10), there is no substantial shared structural feature among these species. Here, the disclosed representative species fail to describe all members of the recited genus of compounds, particularly in view of the widely variant species with respect to both structure and function that are encompassed by the genus. Given the lack of description of a representative number of compounds to reflect the variation among the members of the genus, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.



**[17]** The scope of enablement rejection of claim(s) 12, 17, 21-22, 31, 36, and 40 are rejected under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See [16] beginning at p. 8 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: Beginning at p. 10 of the instant remarks, applicant argues the examiner has mischaracterized the state of the art at the time of the invention, asserting "a wide variety of agents known in the art to activate AMPK" was known at the time of invention, referring to the references cited in support of applicant's position addressing the written description rejection. Applicant argues that the specification and literature provide extensive examples of AMPK activators that were known at the time of the invention that vary across structure and function.

Applicant's argument is not found persuasive. With respect to the references relied upon at pp. 8-9 of the instant remarks, as noted above, the application claims the benefit of domestic priority to provisional applications filed in 2003. However, the references cited in support of applicant's position appear to have been made publicly available only after the time of filing, *i.e.*, 2006 or later. As such, these references do not appear to support applicant's assertion that "a wide variety of agents known in the art to activate AMPK" was known at the time of invention.

While it is acknowledged that the specification discloses compounds that are asserted to have the function of increasing AMPK activity or activating AMPK, these working examples in combination with the remaining disclosure fail to enable the *full* scope of recited compounds, which, as noted above, includes (but is not limited to)

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small molecule organic compounds, peptides, polypeptides, antibodies, and nucleic acids, which act directly or indirectly to increase AMPK activity or activate AMPK. This interpretation is supported by applicant's instant remarks, noting that activators of AMPK "include small organic molecules, peptides, polypeptides, nucleic acids, and fatty acids" (instant remarks at p. 8, bottom) and includes compounds that, *e.g.*, induce AMPK expression (instant remarks at p. 7, middle).

Applicant also argues the examiner acknowledges the experimentation required to screen for compounds that activate AMPK or increase AMPK activity were known and supports the position that only routine experimentation is required to identify the recited compounds.

Applicant's argument is not found persuasive. While it is true that assays for identifying compounds that activate or increase AMPK activity were known, *e.g.*, AMPK kinase assay, these assays are useful for identifying compounds that have a direct effect on AMPK kinase activity. However, as noted above, the claims are not so limited to compounds that directly affect AMPK kinase activity. Instead, the scope of recited compounds broadly encompasses *any* compound having *any* effect that results in activation or increase in AMPK activity. Thus, a skilled artisan is left to experiment to identify assays for making all compounds that are encompassed by the claims.

The examiner maintains the position that in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the significant amount of non-routine experimentation required, undue experimentation would be necessary for a skilled artisan to make and

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use the entire scope of the claimed invention. As such, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

### ***Claim Rejections - 35 USC § 102***

**[18]** The rejection of claims 31 and 40 under 35 U.S.C. 102(b) as being anticipated by Shen et al. (*Clin. Cancer Res.* 8:2085-2090, 2002; hereafter referred to as “Shen”) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See [17] beginning at p. 11 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: Beginning at p. 12 of the instant remarks, applicant argues that while Shen teaches the result of recombinant expression of LKB1 in an *LKB1*-negative cell line is growth inhibition, Shen does not disclose the result is promoting apoptosis and thus cannot anticipate the claimed method.

Applicant's argument is not found persuasive. There is no dispute that the expression vector encoding LKB1 of Shen is a “compound that is an activator of AMP-activated protein kinase” as encompassed by the claims. What is in dispute is whether

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or not Shen practices the claimed method. Applicant takes the position that because Shen does not expressly teach “promoting apoptosis”, then Shen cannot anticipate the claimed method. However, the examiner maintains the position that Shen anticipates the claimed method regardless of whether or not Shen expressly teaches the method promotes apoptosis. Claims 31 and 40 require a single active method step, *i.e.*, contacting the cells with a compound that is an activator of AMPK. As noted in the prior Office action, the reference of Shen teaches the cell line MDA-MB-435 lacks the *LKB1* gene (p. 2085, column 2, bottom) and teaches transfection with an expression vector encoding LKB1 polypeptide (p. 2085, column 2, bottom). Thus, Shen teaches the single active step of the claims.

It appears applicant takes the position that Shen must expressly teach the result of such action is promoting apoptosis, however, the phrase “promoting apoptosis” appears in the preamble of the claim and has been interpreted in accordance with MPEP 2111.02.II as a purpose or intended use of the claimed method. Moreover, even if the claims required promoting apoptosis, this would be a necessary result of practicing the method of Shen. As noted in MPEP 2112.02, “When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process”. Since the Office does not have the facilities for examining and comparing applicant’s method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of Shen (*i.e.*, that the method of Shen

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does not promote apoptosis). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

***Claim Rejections - 35 USC § 102/103***

[19] The rejection of claims 12, 17, 21, 31, 36, 40, and 71-72 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Dilman et al. (*Arch Geschwulstforsch* 48:1-8, 1978; “hereafter referred to as “Dilman1”) OR Dilman et al. (*Gerontology* 26:241-246, 1980; hereafter referred to as “Dilman2”) as evidenced by Shen (*supra*) and Zhang et al. (*Am. J. Physiol. Circ. Physiol.* 293:H457-H466, 2007; hereafter referred to as “Zhang”) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See [17] beginning at p. 11 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: Beginning at p. 13 of the instant remarks, applicant argues the evidentiary reference of Shen fails to provide evidence that the mammary tumors of Dilman1 and Dilman2 necessarily have reduced or absent LKB1 activity.

Applicant’s argument is not found persuasive. With regard to claims 12, 17, 21, and 71, is noted that the claims do not require the subject to have cancer cells with reduced or absent LKB1 activity. Instead, the claims only require the subject have a “cancer *characterized by* reduced or absent LKB1 activity”. Shen identifies LKB1 as a tumor suppressor gene (p. 2085, title and abstract) and teaches “We also demonstrated that low *LKB1* protein expression correlates with higher histological grade..., larger

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tumor size...Furthermore, *LKB1* low expression was associated with a higher relapse rate...and a worse OS...*LKB1* plays a role in tumor suppressor function in human breast cancer” (p. 2085, abstract). Thus, regardless of whether or not MDA-MB-435 and MDA-MB-231 cells are of breast cancer origin, one of ordinary skill in the art in reading the reference of Shen would clearly recognize that breast cancer is a “cancer *characterized by reduced or absent LKB1 activity*” (emphasis added). Since breast cancer is a “cancer *characterized by reduced or absent LKB1 activity*”, the mammary tumors of the Dilman references are considered to be cancers “*characterized by reduced or absent LKB1 activity*”.

Also, as noted above, the phrase “cancer characterized by reduced...*LKB1 activity*” in claims 12, 17, 21, and 71 and the phrase “cells having reduced or absent *LKB1 activity*” are relative terms and there is no reference *LKB1 activity* in the claims such that one of ordinary skill in the art can determine whether or not the recited “cancer” or “cells” are or are not encompassed by the claims and in the interest of giving the claims their broadest reasonable interpretation, the mammary tumors of the Dilman references are considered to be encompassed by “a cancer characterized by reduced or absent *LKB1 activity*” or “cells having reduced or absent *LKB1 activity*”.

**[20]** The rejection of claim 22 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Dilman<sup>1</sup> OR Dilman<sup>2</sup> as evidenced by Shen and Zhang and as further evidenced by Caraci et al. (*Life Sci.* 74:643-650, 2003; hereafter referred to as “Caraci”) is maintained for the reasons of record and the

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reasons set forth below. The rejection was fully explained in a prior Office action. See [19] beginning at p. 14 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: Beginning at p. 14 of the instant remarks, applicant argues the reference of Dilman1 or Dilman2 fails to anticipate claim 12 for reasons noted above.

Applicant's argument is not found persuasive. As noted above, at least in view of a broad and reasonable interpretation of the phrases "a cancer characterized by reduced or absent LKB1 activity" or "cells having reduced or absent LKB1 activity", the reference of Dilman1 or Dilman2 anticipates claim 12.

Applicant further argues claim 22 recites two active steps, requiring a combination treatment that is different from a single treatment, *e.g.*, administering phenformin.

Applicant's argument is not found persuasive. Applicant takes the position that a single step cannot encompass both "administering" and "subjecting" as required by claim 22. However, claim 22 does not exclude administering phenformin to a subject to achieve "a cell death stimulus" and there is no dispute that administering phenformin to the mammary tumors of Dilman1 or Dilman2 achieves a cell death stimulus. The step of "further comprising subjecting the cancer of the subject or cells thereof to a cell death stimulus" in claim 22 has been broadly and reasonably interpreted as encompassing administering phenformin to achieve a cell death stimulus. Thus, the single step of administering phenformin as required by claim 12, which also has the action of "subjecting the cancer of the subject or cells thereof to a cell death stimulus",

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anticipates claim 22. To interpret claim 22 as excluding a single step that encompasses both “administering” and “subjecting” would apply an overly narrow interpretation of the claim.

***Claim Rejections - 35 USC § 103***

[17] The rejection of claims 12, 17, 21-22, 31, 36, 40, and 71-72 under 35 U.S.C. 103(a) as being unpatentable over the combination of Dilman1, Dilman2, and Dilman et al. (*Cancer Lett.* 7:357-361, 1979; hereafter referred to as “Dilman3”) as evidenced by Shen, Zhang, and Caraci is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See [17] beginning at p. 15 of the Office action mailed on 4/14/09.

RESPONSE TO ARGUMENT: Beginning at p. 15 of the instant remarks, applicant argues that the benefit of increasing AMPK activity in tumors having reduced or absent LKB1 activity was unexpected. According to applicant, this unexpected result supports a finding of non-obviousness, at least because one of ordinary skill in the art could not have had a reasonable expectation of success in making the claimed invention without prior knowledge of the benefit of increasing AMPK activity for tumors having reduced or absent LKB1 activity. Applicant argues that the tumors treated in the Dilman references is not disclosed as having reduced or absent LKB1 activity and the combination of Dilman references fails to teach phenformin has an effect on cancers characterized by reduced or absent LKB1 activity, that phenformin promotes apoptosis of cells having reduced or absent LKB1 activity, or that tumors that have reduced or



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absent LKB1 activity would benefit from administering phenformin. According to applicant, the Office's position that one would have been motivated to administer phenformin to a patient having a cancer characterized by reduced or absent LKB1 activity or to promote apoptosis of cells having reduced or absent LKB1 activity is based purely on hindsight reasoning.

Applicant's argument is not found persuasive. Contrary to applicant's position, the expected benefits of administering phenformin to a cancer patient, *e.g.*, reducing tumor incidence, reducing tumor growth, and potentiating the antitumor effect of anti-cancer therapies, were well-known at the time of the invention as shown by the teachings of the Dilman references and are reasonably expected in view of the prior art. Although the teachings of the Dilman references do not appear to specifically direct one to administer phenformin to a patient with a cancer having reduced or absent LKB1 activity, based on the teachings of the Dilman references that the benefits of phenformin are broad-based and not limited to any particular type of kind of cancer, one would have been motivated to administer phenformin to a patient having *any type or kind of cancer*. In other words, in view of the teachings of the Dilman references, one of ordinary skill would have been motivated to administer phenformin to *all types and kinds of cancer* and there is no teaching or suggestion to teach away from administering phenformin to a subpopulation of cancer patients having cancers with reduced or absent LKB1 activity. Moreover, in view of the teachings of the Dilman references, one would have reasonably expected a beneficial result as a consequence of administering phenformin to a patient having *any type or kind of cancer*. The expected beneficial results of

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administering phenformin are taught by the Dilman references and do not require a *priori* knowledge of a nexus between AMPK and LKB1 to practice administering phenformin to a subject having any type or kind of cancer. Also, while the teachings of the Dilman references do not appear to disclose phenformin as increasing AMPK activity in a subject having a cancer with reduced or absent LKB1 activity or to promote apoptosis in cells having reduced or absent LKB1 activity, this is a necessary result of administering phenformin to a subject having such a cancer or to such cells.

### **Conclusion**

**[21]** Status of the claims:

- Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are pending.
- Claims 12, 17, 21-22, 31, 36, 40, and 71-72 are rejected.
- No claim is in condition for allowance.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/  
Primary Examiner, Art Unit 1656